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Stryker's Sustainability Solutions Reprocessed LigaSure Curved, Small Jaw, Open Sealer/Divider (LF1212A) and Remanufactured LigaSure Exact Dissector, Without Nano-coating (LF2019):

A Pre-Clinical Comparison to OM LigaSure Curved, Small Jaw, Open Sealer/Divider and Exact Dissector, Nano-coated

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Study summary

Stryker's Sustainability Solutions (SSS) reprocessed/remanufactured LF2019 and LF1212A devices were compared to the original manufacturer (OM) devices and **found to perform as well as OM devices for seal integrity (hemostasis) and tissue sticking in an acute study. Thermal spread measurements were also found to be statistically equivalent between OM and reprocessed/remanufactured devices using histopathology methods.** The average thermal spread depth for reprocessed LF1212A devices was 2.53mm, and 2.37mm for OM LF1212A devices, and the thermal spread width was 4.49mm and 4.46mm, respectively. The average thermal spread depth for remanufactured LF2019 devices was 4.315mm, and 4.370mm for OM LF2019 devices. For thermal spread width the average was 2.07mm and 2.02mm, respectively. Additionally, a chronic, 21-day animal survival study was performed, which demonstrated effective long-term seal quality of the reprocessed/remanufactured devices (pertains to both LF1212A and LF2019). The pathological gross assessment of the surviving animals demonstrated healed vascular seal sites with acceptable long-term seal quality and no indication of recent or active bleeding. In addition, there were no hemostatic complications or evidence of thermal injury to adjacent tissue attributed to use of the reprocessed/remanufactured devices for both models (LF1212A and LF2019).

Background

Advanced directed energy vascular sealing instruments have become essential with the proliferation of endoscopic procedures, as well as general surgical procedures. These devices are of vital importance to providing hemostasis while sealing and dividing vessels. **With over two decades of reprocessing experience, Stryker's Sustainability Solutions business is the market-leading provider of reprocessing services for medical devices. Reprocessors of single-use medical devices must demonstrate "substantial equivalence" to a legally marketed (predicate) device through Premarket Notification, or 510(k) clearance, in accordance with the Food and Drug Administration (FDA) Code of Federal Regulations (21CFR Part 807).[1] Specifically, FDA guidance for bipolar electrosurgical vessel sealers suggests that comparative thermal spread data should be provided that includes quantitative measurement (under magnification) of the size (depth and width) of the thermal damage zone.** After vessels are sealed with either subject or predicate (control) device, thermal damage (e.g. coagulation necrosis) should be assessed histologically to determine the distance from the edge of the seal.

Similarly, the same guidance states that in order to assess the long-term seal quality and potential for injury to adjacent structures, a chronic animal study should evaluate device performance at a minimum of three (3) weeks post-procedure in at least five (5) animals.[2] **As part of the verification and validation activities conducted to demonstrate substantial equivalence to the predicate, acute and chronic animal studies were designed and executed in a porcine model in accordance with the FDA guidance. The results of the seal integrity evaluation are outlined in the succeeding discussion.** A passing result is defined as no difference in performance between reprocessed/remanufactured and OM devices for both acute and chronic studies.

Method

The preclinical studies consisted of American Preclinical Services (APS) approved protocols using a porcine model[3,4]. The anatomy and physiology of the porcine model provided a tissue response to electrosurgical instrumentation similar to that of human tissues. The surgeon and pathologist were blinded as to the device identification (OM vs. reprocessed/remanufactured) until after all scoring, measurements and gross evaluation were completed to eliminate bias.

The chronic, 21-day survival study was designed to assess long-term seal quality and potential for injury to adjacent structures. Multiple vessel types and diameters per animal were sealed using reprocessed/remanufactured and OM LigaSure LF1212A and LF2019 devices. For the chronic, 21-day survival study, a total of six (6) subject animals (where one reprocessed/remanufactured device was used for each subject), plus one (1) control animal (OM device was used) underwent a splenectomy, unilateral nephrectomy and bilateral oophorectomy, and all vessels associated with the organs were sealed with a LigaSure LF1212A device (six reprocessed plus one OM device). A gross evaluation was performed at day 21 to assess hemostasis of the sealed vessels and any collateral tissue changes, as appropriate. Similarly, the same amount of devices and animals (different set of animals than used for LF1212A devices) were used for the LF2019 devices.

The acute animal study was designed to compare four (4) subject animals and three (3) control animals, where a total of seven (7) porcine test systems were used for the LF1212A model study. For the LF2019 model study three (3) subject animals and three (3) control animals for a total of six (6) porcine test systems were used. One reprocessed/remanufactured device was used for each subject animal and one OM device was used for each control animal. Each animal underwent procedures to seal multiple vessels of different sizes and with various physiological functions as indicated in Table 1. Device performance was assessed through thermal spread measurement, seal integrity (hemostasis), and tissue sticking to the device jaws.

Vessel type	Vessel identification
A/V bundle	Ovarian pedicle, short gastric, splenic, uterine bundle
Artery	Carotid, gastric splenic, large intestinal, rectal, renal, small mesenteric, splenic
Vein	Gastric splenic, internal jugular, large intestinal, rectal, renal, small mesenteric, splenic

Table 1. Vessel type and identification

In the acute study, thermal spread depth and thermal spread width were measured postoperatively and evaluated by an APS board-certified veterinary pathologist. As seen in Figure 1, the thermal spread length (depth) (indicated by the double headed arrow) was measured as the distance from the outside or outer edge of the thermal injured tissue/seal (indicated by the dotted arrow) to the endpoint of thermal change (indicated by the broken arrow). The measurements were obtained from the intimal, medial or adventitial surface of the blood vessel or vascular plexus.

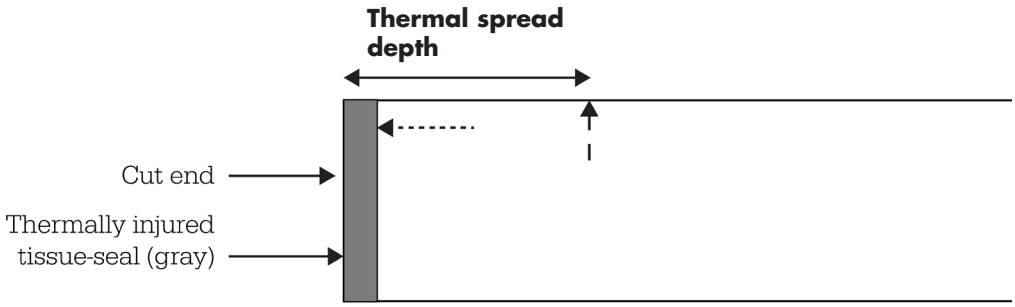

Figure 1. Depth of thermal spread measurement

The width of thermal spread (indicated by the double-headed arrow) in Figure 2 was the measured distance from the thermally injured perivascular tissue on one side of the vessel (light gray area) to the thermally injured tissue on the opposite side of the vessel. The measurement was obtained at approximately halfway between the inner edge of the thermal seal and the endpoint of the thermal injury.

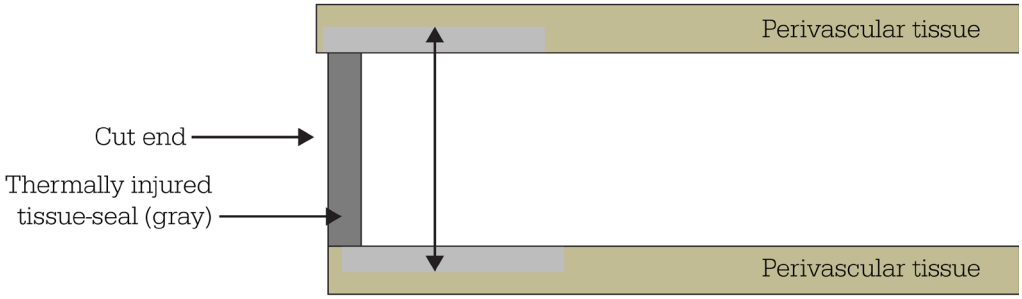

Figure 2. Width of thermal spread measurement

When comparing the data sets between OM and reprocessed/remanufactured devices for thermal spread depth and thermal spread width, statistical methods such as a two-sample t-test or Mann-Whitney comparison test were used to see if the data sets were different. When utilizing one of these statistical methods for comparison between the data sets, a p-value greater than 0.05 indicates that there is not a detectable statistical difference between populations; thus, showing equivalence between the OM and reprocessed/remanufactured devices.

For tissue sealing (hemostasis) during the acute study, a scoring code was used for visual confirmation of maintained tissue sealing after one (1) minute and ten (10) minutes ‡. A similar scoring code was used for the tissue sticking assessments of the tissue sticking to the jaws of the devices ‡. Assessments were made by the surgeons during the vessel sealing procedures. For seal integrity and tissue sticking, descriptive statistics comparison was done to compare the median of the scoring assessments taken from all the reprocessed/remanufactured devices compared to the median of the scoring assessments for all the OM devices used during the procedures. The raw data and detailed statistical analysis are contained in the report on file[3,4].

Results

The LigaSure LF1212A and LF2019 devices are indicated for sealing vessels (arteries and veins) up to and including seven (7) mm. Table 2 and Table 3 below gives the summary of all the vessels sealed during the acute study for the LF1212A and LF2019 devices. There is no statistical difference when comparing vessel sizes from what the reprocessed/remanufactured and OM devices sealed.

Vessel size	LF1212A test arteries sealed	LF1212A test veins sealed	LF1212A test AV bundles sealed	LF1212A OEM arteries sealed	LF1212A OEM veins sealed	LF1212A OEM AV bundles sealed
1mm	0	2	6	2	0	8
2mm	8	2	4	1	2	6
3mm	1	10	7	7	6	6
4mm	4	3	10	4	5	3
5mm	10	7	5	6	2	6
6mm	8	3	3	5	3	3
7mm	3	2	4	4	2	6

Table 2. LF1212A sealed vessels size distributions (acute study)

Vessel size	LF2019 test arteries sealed	LF2019 test veins sealed	LF2019 test AV bundles sealed	LF2019 OEM arteries sealed	LF2019 OEM veins sealed	LF2019 OEM AV bundles sealed
1mm	0	4	5	1	4	1
2mm	4	1	7	6	3	7
3mm	5	4	8	5	7	8
4mm	9	6	9	4	4	2
5mm	6	3	9	14	4	9
6mm	3	2	0	2	7	6
7mm	1	1	2	0	1	2

Table 3. LF2019 sealed vessels size distributions (acute study)

Acute study thermal spread

For thermal spread width and thermal spread depth, one hundred and one (101) data points were able to be captured with the four reprocessed LF1212A devices used from the four subject animals; while eighty-five (85) data points were obtained from the three OM LF1212A devices used for the three animals assigned for those OM devices. Meanwhile for the LF2019 model study, eighty eight (88) data points were able to be captured with the three remanufactured LF2019 devices used from the three subject animals; while ninety-four (94) data points were obtained from the three OM LF2019 devices used for the three animals assigned for those OM devices. **Each specimen was microscopically measured (morphometry) by the pathologist and the data was sent to the study sponsor for statistical analysis per the protocol. There was no statistical difference between the OM and reprocessed populations for either thermal spread depth or thermal spread width** as stated in Table 4. All statistical analysis can be found in SSS internal reports.[3,4]

Device	Total samples (N)	Thermal spread depth (mm)	P-value: thermal spread depth	Thermal spread width (mm)	P-value: thermal spread width	Results
Reprocessed LF1212A	101	2.45	0.3787	4.49	0.697	PASS: Statistical Equivalence
OM LF1212A	85	2.38		4.61		
Remanufactured LF2019	88	4.315	0.772	2.07	0.7387	PASS: Statistical Equivalence
OM LF2019	94	4.370		2.02		

Table 4. LigaSure reprocessed/remanufactured vs. OM LF1212A and LF2019 devices for thermal spread

Histology

Figures 3 and 4 represent the manner in which the histological slides were measured for the depth of thermal tissue spread. The figures are not meant to compare the thermal spread values or images to each other as they are different vessel types. Arrows in Figures 3 and 4 indicate the intact seals.

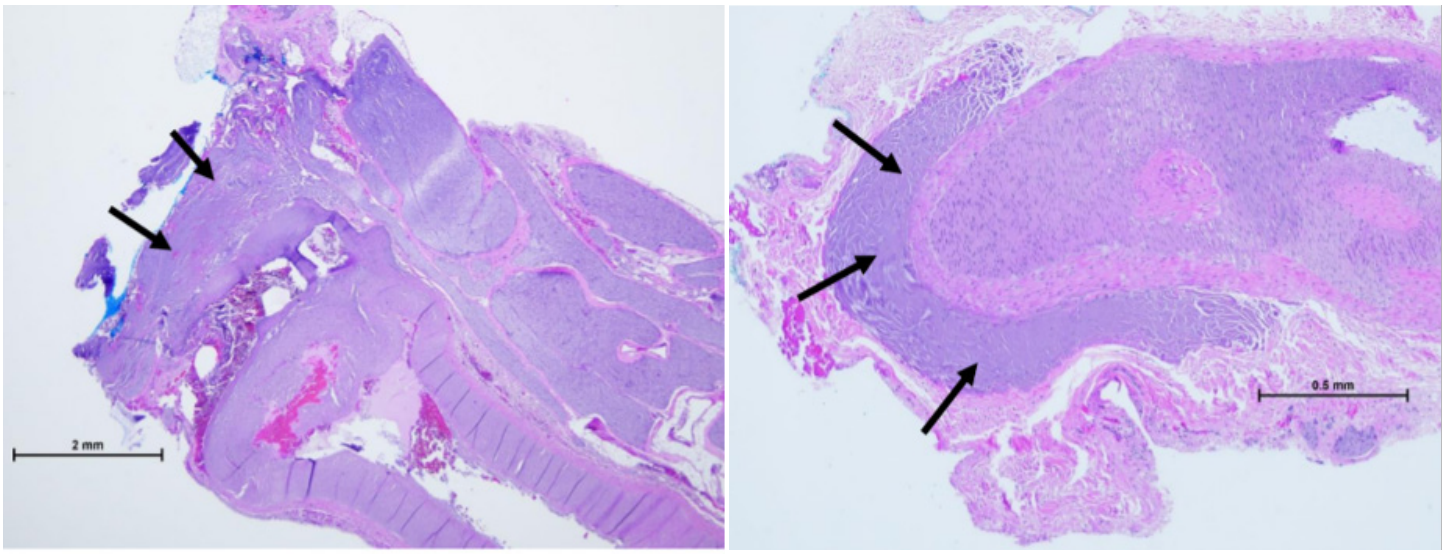

Figure 3. Reprocessed LF1212A seal on a renal artery vs. OM LF1212A on gastric artery

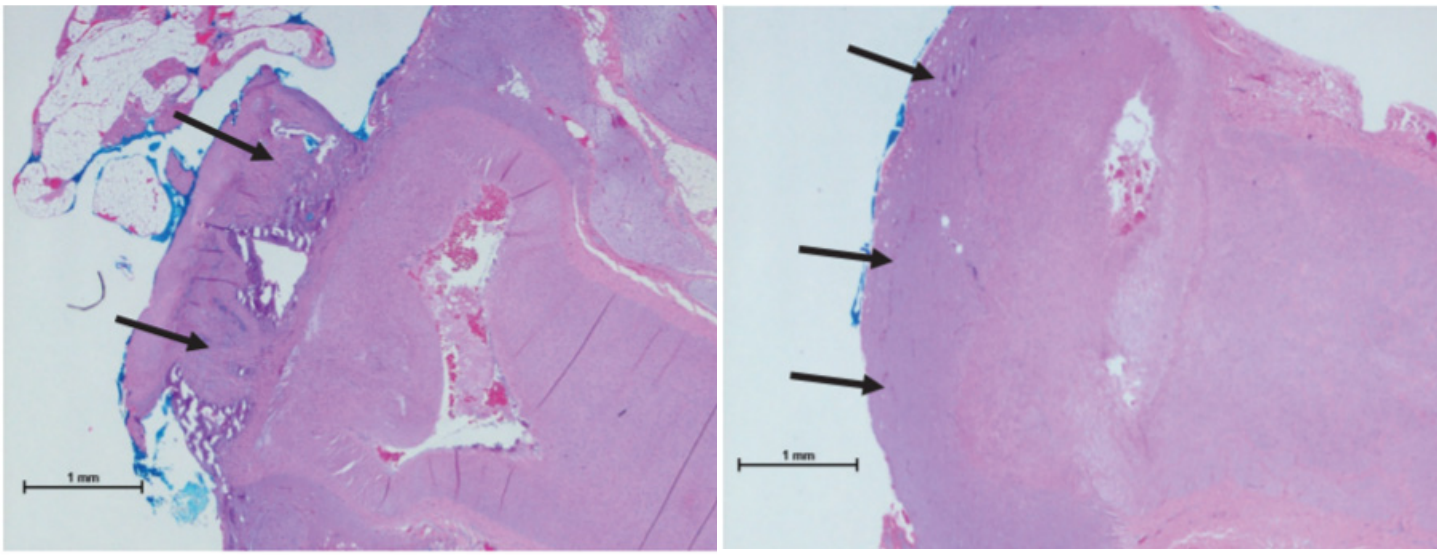

Figure 4. Remanufactured LF2019 seal on a splenic artery vs. OM LF2019 on renal artery

Seal integrity

For seal integrity, one hundred and three (103) data points were obtained for reprocessed LF1212A devices, and eighty-seven (87) data points for OM LF1212A devices. Eighty-nine (89) data points were obtained for remanufactured LF2019 devices, and ninety-seven (97) data points for OM LF2019 devices. Seal integrity data points were made up of seal integrity (any leaking) assessments made at the one minute and ten minute mark after sealing the vessel ‡. **There was no statistical difference between the reprocessed/remanufactured and OM data groups. The average seal integrity rating for both reprocessed/remanufactured and OM was 1.00, indicating adequate seal at tissue site with no leakage of blood (complete hemostasis) as evaluated by the surgeon, and according to the established ranking scale. At all seal sites, the vessel was closed or sealed and there was no evidence of hemorrhage, vascular leakage or fibrin deposition on the ends. Additionally, there was no loss of vascular structure, such as arterial dissection or arterial/venous medial thinning observed in any site (OM or reprocessed/remanufactured).** All statistical analysis can be found in SSS internal reports.[3,4]

Tissue sticking

When comparing LF1212A devices, one hundred and two (102) reprocessed data points and seventy-four (74) OM data points were evaluated for tissue sticking by the surgeon when performing sealing on the vessels. Eighty-nine (89) data points were obtained for remanufactured LF2019 devices, and ninety-seven (97) data points for OM LF2019 devices. **Overall average for both the reprocessed/remanufactured and OM ranking for tissue sticking was 1.00, indicating no tissue sticking as tissue falls off the device when opened. Descriptive statistics comparison was done and yielded no difference in the mode or median for the tissue sticking assessments.** All statistical analysis can be found in SSS internal reports.[3,4]

Chronic study

At 21-day necropsy, the pathological gross assessment of the surviving animals demonstrated healed vascular seal sites with acceptable longterm seal quality and no indication of recent or active bleeding. **In addition, there were no hemostatic complications or evidence of thermal injury to adjacent tissue attributed to use of the reprocessed/remanufactured device. The chronic study provides further assurance that the remanufactured LigaSure devices (LF1212A and LF2019) will perform as intended to provide acceptable long-term seal quality and is safe for human use.**

Conclusion

The reprocessed/remanufactured devices that were compared to brand new models (OM LF1212A and OM LF2019) during the acute and chronic animal studies demonstrated long-term seal quality. The data analyzed for thermal spread, tissue sealing and tissue sticking showed statistical equivalence between the reprocessed and OM devices. This demonstrates that the reprocessed/remanufactured devices performed comparably to the OM devices with regards to device usability, performance, and thermal spread in the acute and chronic in vivo porcine model. Data from these acute and chronic in vivo studies were provided as part of an FDA 510(k) pre-market notification.

‡ The four-tiered scoring code used for the visual assessments were as follows:

Evaluation	Scoring code
Seal integrity	1- Seal at treatment site, no blood or lymph leakage
	2- Seal at treatment site, with slight oozing of blood or lymph that stops within 1 minute ± 15 seconds
	3- Partial sealing, with brisk blood or lymph leakage present that requires intervention
	4- Incomplete sealing, with uncontrolled blood or lymph leakage requiring intervention
Tissue sticking	1- No sticking, tissue falls off instrument when opened
	2- Tissue sticking, minor adherence to one or both jaws
	3- Tissue sticking, requiring counter tension and extensive force to remove tissue
	4- Tissue sticking such that tissue is damaged or torn during the removal process

References

1. 21 CFR Part 807, Subpart E, Premarket Notification Procedures.
2. Draft Guidance for Industry and Food and Drug Administration Staff, Premarket Notification [510(k)] Submissions for Bipolar Electrosurgical Vessel Sealers for General Surgery, Issued March 24, 2014
3. Reports on file. TR20956 Engineering Study Report Design Validation Study (Acute, Chronic, and Lymphatic GLP) for LigaSure Small Jaw (LF1212A); and TR21208 Statistical Analysis for Acute Animal Study on Reprocessed LigaSure Small Jaw, LF1212A
4. Reports on file. TR21190 Engineering Study Report Design Validation Study (Acute, Chronic, and Lymphatic GLP) for LigaSure Exact Dissector (LF2019); and TR21209 Statistical Analysis for Acute Animal Study on Remanufactured LigaSure Exact Dissector (LF2019)